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09/909,556	07/20/2001	Eva-Maria Franken	Mo-6470/LcA 34,772	4311

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BAYER CROPSCIENCE LP  
Patent Department  
100 BAYER ROAD  
PITTSBURGH, PA 15205-9741

EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 03/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/909,556

Applicant(s)

FRANKEN ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 28 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 1-14, 16 and 18-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15, 17 and 21-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 06/17/2002
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Status of Claims***

1. Response to restriction requirement filed 11/28/2003 is acknowledged. Applicant elected, Group VI, claims 15,17,21-23. Insofar as applicants have not specifically pointed out the reasons supporting the statement of the traversal, applicants' election is taken to be without traverse. See MPEP 818.03(a). The requirement is still deemed proper and is therefore made FINAL. Claims 1-14,16,18-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups. Cancellation of claims 1-14,16,18-20 is requested.

### ***Information Disclosure Statement***

2. Applicants' Information Disclosure Statement filed 06/17/2002 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1)

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states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Please, (1) remove the list from specification, and (2) remove numerical numbering of references in the text of specification.

***Sequence Listing***

4. The Sequence Listing was approved by STIC for matters of form.

***Claim Rejections - 35 USC § 112, second paragraph.***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 15,17,21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons:

- A. The term "structures capable of undergoing interactions " is vague and indefinite. In which case a compound is deemed of being capable to interact ? The term is indefinite because it is a relative term, but no standard of reference has been

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provided with which to determine whether a particular compound is deemed capable of interacting.

B. The term "specific" in the phrase "specific interactions" is vague and indefinite. What constitutes "specific" interaction - is it any hydrogen bond, covalent bond, or ionic bond? The term is indefinite, and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

C. The claims are confusing in reciting limitation of "computer-aided modeling". As the claims do not specify what particular method steps are involved, it is unclear what is intended to be done. The claim does not provide sufficient information as to how or under what circumstances such a limitation would be made.

D. The claims refer to ligand-binding domain according to claim 1; the latter, however, is drawn to non elected invention. Please amend the claims to recite the claimed subject matter in full.

E. Further, in reciting ligand-binding domain according to claim 1, the claims address not a certain set of coordinates of molecular structure, but rather a crystallized molecular fragment. It is not clear how a three-dimensional image of a crystallized molecular fragment (e.g, a photograph of a crystal) can be useful in molecular modeling.

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***Claim Rejections - 35 USC § 112, first paragraph.***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 15,17,21-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The instant invention is drawn to method of finding USP ligands by identifying structures that are capable of interacting with 3-D image of crystallized ligand-binding site of USP.

The state of the art and predictability of the prior art.

As disclosure informs, USP is an orphan receptor for which no ligand is known. Therefore, the art is deemed to be unpredictable.

The presence or absence of working examples

The specification is devoid of any examples of the claimed method.

The amount of direction or guidance present

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There is no guidance on the meaning of the term "structures capable of undergoing specific interactions with LBD". The intended meaning and scope of being capable of undergoing specific interactions is not clear. No method steps directed at identifying structures being capable of undergoing specific interactions are disclosed.

Further, the instant claims are not drawn to use three-dimensional image based on molecular coordinates of the domain of interest. Rather, as the claims refer to "LBD according to claim 1", the claims address not a certain set of coordinates of molecular structure, but rather an image of a crystallized molecular fragment. Thus, the claims may be viewed as reading on using a conventional photograph of a crystal for design of ligands interacting with particular molecular configuration. Clearly, specification does not provide guidance on such method of modeling of ligands.

Consequently, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make the invention with the claimed breadth without an undue amount of experimentation.

7. Further, even if claims 15,17,21-23 had been enabled in spite of the reasons set forth in the previous paragraph, the claims while being enabling for methods of modeling ligands to USP derived from *Heliothis virescense*, would not reasonably

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provide enablement for methods of modeling ligands to USP derived from other sources. The method is based on information obtained from 3-D modeling of the crystal structure obtained for USP derived from *Heliothis virescense*. There are no data for USP derived from any other sources. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

***Claim Rejections - 35 USC § 103.***

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).



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8. Claims 15,17,21-23 are rejected under 35 U.S.C. 103(a) as obvious over US 6110698 in view of US 6236496 or WO 99/50568 (the latter reference is submitted by applicant in IDS filed 12/24/2002).

The instant claims are drawn to method of finding USP ligands by generating three-dimensional image of ligand-binding site of USP, and performing computer-aided modeling to identify structures that are capable of interacting ligand-binding site of USP<sup>1</sup>.

US 6110698 teaches that ultraspiracle protein (USP) is an insect orthologue of vertebrate retinoid receptor that might be involved in the ecdysone (Ec) response pathway of metamorphoses and imaginal disk formation. USP also functions in insect female reproduction and eye morphogenesis, and may participate in Ec-dependent and Ec-independent processes in the fly. These properties of USP implicate it as an important target for insecticides. In particular, the role of USP in insect development, and the differences between USP and vertebrate RxR proteins, implicate it as a target for environmentally safe compounds that act as insect growth regulators. (See Background section). The reference describes a method for identifying compounds that inhibit the function of USP by incubation of test compounds with transformed

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<sup>1</sup>Note that the claims are not drawn to any particular set of crystal coordinates (e.g., such as those in claim 5).

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yeast cells containing USP and reporter gene and monitoring reduction in the the expression of the reporter gene in the test culture relative to the control culture. The reference, while teaching the need to identify USP ligands does not teach *in silico* methods of identifying such ligands. It would be obvious to one skilled in the art, however, that computerized *in silico* methods of identifying the desirable ligands would significantly empower and simplify search of such ligands.

US 6236496 or WO 99/50568 teach such representative methods of computer-aided design of nuclear receptor synthetic ligands. The references teach methods of designing a nuclear receptor synthetic ligand comprising steps of generating three-dimensional image model of protein comprising a ligand-binding domain (LBD) and performing modeling of compounds that are capable of interacting with LBD.

It would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to use computer-aided method of US 6236496 or WO 99/50568 to design ligands of USP because such ligands are of interest as potential insecticides and because use of a computer-aided ligand design method would significantly empower and simplify search of such ligands.

In regard to claims 21,22 drawn to methods of finding active compounds for crop protection, it would be obvious that because USP ligands are can potentially be used as insecticides, they will be of interest to be used for crop protection.

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In regard to claim 23, drawn to method of finding effectors of gene expression, US 6110698 teaches that USP is nuclear receptor involved in regulation of gene expression, and teaches method of identifying USP ligands as effectors of gene expression by determining changes in gene expression caused by the USP ligands.

9. If claims 15,17,21-23 are amended to recite any particular 3-D coordinates of the lipid-binding domain, the following rejection is also applied.

Claims 15,17,21-23 are rejected under 35 U.S.C. 103(a) as obvious over US 6236496.

US 6236496 teaches method of computer-aided design of nuclear receptor synthetic ligand comprising steps of generating three-dimensional image model of protein comprising a ligand-binding domain (LBD) and performing modeling of compounds that are capable of interacting with LBD.

The current claims are drawn to method of computer-aided design of nuclear receptor synthetic ligand which rely upon particular three-dimensional coordinates of the lipid binding domain of USP. However, as MPEP 2106 notes,

"Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. Cf. *In re Gulack*, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) (when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art

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in terms of patentability). Common situations involving nonfunctional descriptive material are:

- a computer-readable storage medium that differs from the prior art solely with respect to nonfunctional descriptive material, such as music or a literary work, encoded on the medium,
- a computer that differs from the prior art solely with respect to nonfunctional descriptive material that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer), or
- a process that differs from the prior art only with respect to nonfunctional descriptive material that cannot alter how the process steps are to be performed to achieve the utility of the invention.

Thus, if the prior art suggests storing a song on a disk, merely choosing a particular song to store on the disk would be presumed to be well within the level of ordinary skill in the art at the time the invention was made. The difference between the prior art and the claimed invention is simply a rearrangement of nonfunctional descriptive material."

In the instant case, the coordinates of LBD of USP is nonfunctional descriptive material which does not distinguish the invention from the prior art. Therefore, the prior art, US 6236496, teaches all of the functional elements of the claims.

#### ***Conclusion.***

10. No claims are allowed

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

February 27, 2004

MICHAEL BORIN, PH.D  
PRIMARY EXAMINER

mlb

A handwritten signature in black ink, appearing to read 'Michael Borin', is written over the printed name and title.